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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,276	09/18/2006	Hans-George Frank	37998-237467	4241

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EXAMINER	
GUPTA, ANISH	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
05/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,276	FRANK ET AL.	
	Examiner	Art Unit	
	ANISH GUPTA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *9-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/2007; 12/11/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-8, and the species TYSCHFGPLTWVCKPQ, in the reply filed on 2/18/2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II-V, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/18/2010.

Specification

2. The abstract of the disclosure is objected to because the specification contains sequences without the corresponding sequence identifier next to the sequence. 37 CFR 1.821(d) states "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." Thus, in order to comply with 37 CFR 1.821(d), Applicants are requested to place the sequence identifiers next the corresponding sequence. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: that actual steps involved in generating an iosseteric structure. The claims state a method of generating an isosteric structure of a polypeptide at least partially containing D-amino acids from 3D-coordinates and sequence information of an L-configured precursor having an N-terminal amino group or substituted amino group, a C-terminal carboxy group or a carboxy derivative, a backbone and L-amino acid side chains. While the claims recite that the method comprises at least partially replacing backbone CO groups with NH groups and vice versa, while keeping fixed the 3D-coordinates of the precursors L-amino acid side chains, the N-terminal amino group or substituted amino group and the C-terminal carboxy group or carboxy derivative, the claims do not make clear if this method step results in generation an isosteric structure of a polypeptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Chorev et al. (Tibtech 1995).

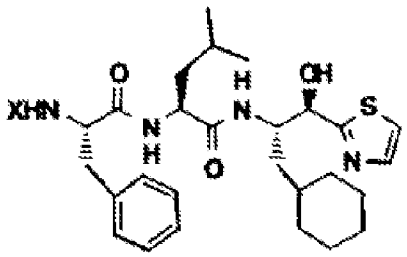
The claims are drawn to a method of generating an isosteric structure of a polypeptide at least partially containing D-amino acids from 3D-coordinates and sequence information of an L-configured precursor having an N-terminal amino group or substituted amino group, a C-terminal carboxy group or a carboxy derivative, a backbone and L-amino acid side chains, and comprising at least partially replacing backbone CO groups with NH groups and vice versa, while keeping fixed the 3D-coordinates of the precursors L-amino acid side chains, the N-terminal amino group or substituted amino group and the C-terminal carboxy group or carboxy derivative.

Chorev et al. teaches methods of generating retro-inverso peptides having all D amino acids (see page 440, right hand column). The reference teaches retro-inverso peptide of CGIRGERA, with N-terminal modifications (see page 441, figure 3). This meets the limitation of claim 2. Note that peptide (d) in figure 3 reverses the CO and NH relative to the L-peptide while keeping the same sterochemistry of the amino acid side-chains. This meets the limitation of claim 1.

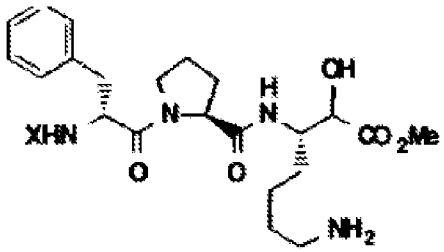
5. Claims 1-3, 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Lau et al. (Bioorganic & Medicinal Chemistry).

The claims are drawn to a method of generating an isosteric structure of a polypeptide at least partially containing D-amino acids from 3D-coordinates and sequence information of an L-configured Lconfigurated precursor having an N-terminal amino group or substituted amino group, a C-terminal carboxy group or a carboxy derivative, a backbone and L-amino acid side chains, and comprising at least partially replacing backbone CO groups with NH groups and vice versa, [[-]] while keeping fixed the 3D-coordinates of the precursors L-amino acid side chains, the N-terminal amino group or substituted amino group and the C-terminal carboxy group or carboxy derivative.

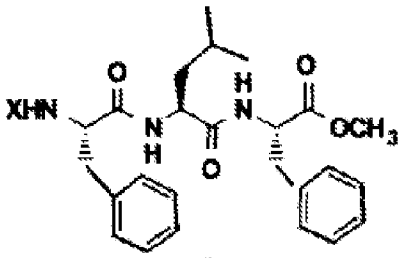
Lau et al. teaches computer assisted design of the tripeptides and their retro inverso variations. Specifically, the reference teaches the retro-inverso peptide which contain all D- amino acids of:



1,2

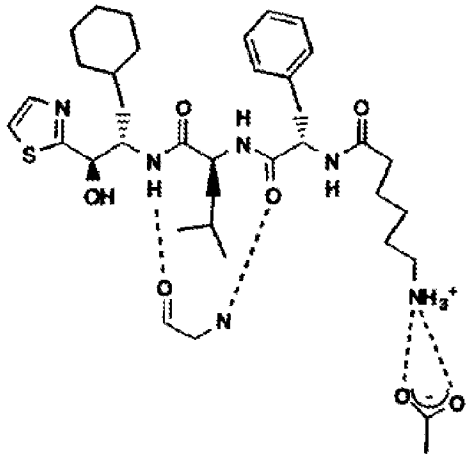


3,4

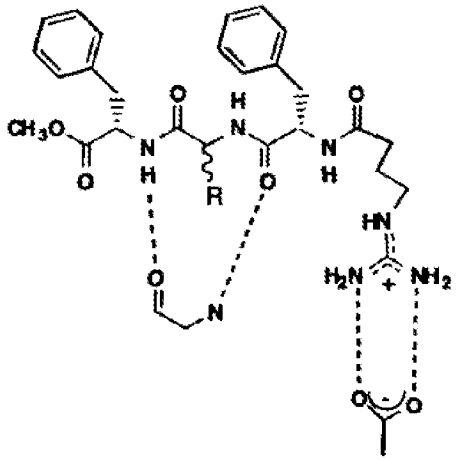


5

The Retro-inverso peptide taught have the structure:



1



6, R =

7, R =

(see page 1042). Note that the retro-inverso peptides have a reversal of the NH and CO groups within the sequence, where CO replaces NH and vice versa relative to their counterparts. The reference discloses structural modification on the terminal end, relative to the counterpart. Namely, the reference discloses that acyaltion of the retropeptides with an alkyl-guanidino or alkyl amino moiety is required for thrombin activity site inhibition (see page 1041). This meets the limitation of claim 2. Reference teaches an all D-amino acid peptide, thereby meeting the limitation of claim 8. The reference states that retro-inverso peptides were modeled using SYBYL (see page 1042). The instant specification, on page 20, teaches that Sybyl modeling software was utilized for the peptide TYSCHFGPLTWVCKPQ. Thus, the reference disclose the use of the same computer modeling system as utilized in the examples of the claimed invention. The instant application also states "[t]he present invention discloses a method for designing a peptide isoster or peptide-like substance based on the coordinates of the structure of a native peptide by the inversion of one ore more (up to all) peptide bonds, comprising steps a –c . . . .Steps a to c can be performed manually by a skilled staff member using the given software utility or can be automatized by appropriate programming of the computer/software unit." See page 6-7. Since the reference disclose the same computer modeling software as that disclosed in the instant application and since the instant application states that the claimed invention can be "performed manually by a skilled staff member using the given software utility, " the reference anticipates the claimed invention.

6. Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodman et al. (Acct. of Chem. Research).

The claims are drawn to a method of generating an isosteric structure of a polypeptide at least partially containing D-amino acids from 3D-coordinates and sequence information of an L-

configured Lconfigurated precursor having an N-terminal amino group or substituted amino group, a C-terminal carboxy group or a carboxy derivative, a backbone and L-amino acid side chains, and comprising at least partially replacing backbone CO groups with NH groups and vice versa, [[-]] while keeping fixed the 3D-coordinates of the precursors L-amino acid side chains, the N-terminal amino group or substituted amino group and the C-terminal carboxy group or carboxy derivative.

Goodman et al. teaches methods of generating retro-inverso peptides having all D amino acids (page 2, figure 3 and page 3). The reference teaches retro-inverso peptide reverss the direction of the peptide bond and inverts the chirality of each chiral center (see page 3). The reference teaches retro peptides containing all D-amino acid residues (See page 4). The reference teaches modification of the terminal group of the retropetpides (see page 4). The reference teaches a Retro-all-D angiotenisn analog where the proline residue is replace by an alanyl or beta-alanine (see page 5, right column). This meets the limitation of claim 4. Since the peptides taught reverses the CO and NH relative to the L-peptide while keeping the same sterochemistry of the amino acid side-chains and since this is the only method step taught within the claims, the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 3, 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wrighton et al. (US5773569) in view of Cherov et al. (Acc. Chem. Res 1993).

The claims are drawn to a method of generating an isosteric structure of a polypeptide at least partially containing D-amino acids from 3D-coordinates and sequence information of an L-configured Lconfigurated precursor having an N-terminal amino group or substituted amino group, a C-terminal carboxy group or a carboxy derivative, a backbone and L-amino acid side chains, and comprising at least partially replacing backbone CO groups with NH groups and vice versa, [[-]] while keeping fixed the 3D-coordinates of the precursors L-amino acid side chains, the N-terminal amino group or substituted amino group and the C-terminal carboxy group or carboxy derivative.

Wrighton teaches the peptide the peptide TYSCHFGPLTWVCKPQ (see table 18, SEQ ID NO 197). The reference also teaches numerous peptides that contain the sequence TYSCHFGPLTWVCKPQ (see table 18). The reference states that peptide TYSCHFGPLTWVCKPQ had an IC 50 value of 2μM in an EPO binding assay (see col. 21-32). The difference between the prior art and the instant application is that the reference does not specifically teach determining isosteric structure of a polypeptide by reversing the CO and NH groups.

However, Goodman teaches benefits of retroinverso peptides and the studies conducted for retro inverso peptides relative to the counterparts. The reference discloses a variety of peptides

including enkephalin, neurotensin, somatostatin, thymopoietin (see page67). The reference teaches Retro-inverso bonds are the most closely related isosteric replacement for the original peptide bond. This modification maintains the major characteristics of the peptide backbone while enabling **(or** providing) a substantial departure from the native structure. Therefore, the potential role of partially modified retroinverso (PMRI) analogs in future peptide-based drug design will be to provide a modification which maintains the polarity and rigidity of a peptidic backbone and contributes its unique conformational preferences and topochemical consequences. Extensive conformational analysis of many constrained retro-inverso analogs of bioactive peptides will significantly contribute to the rational design of peptidomimetic drugs. Most of the PMRI analogs studied displayed not only stability toward enzymatic degradation and bioavailability but also improved potency and selectivity. As such, the retro-inverso modifications of bioactive molecules remain a major challenge for bioorganic chemists (see page 273). It would have been obvious therefore to generate the retro-inverso peptide of TYSCHFGPLTWVCKPQ for studying the structural attributes of the peptide. One would have been motivated to do so because extensive conformational analysis of constrained retro-inverso analogs of bioactive peptides will significantly contribute to the rational design of peptidomimetic drugs. Most of the PMRI analogs studied displayed not only stability toward enzymatic degradation and bioavailability but also improved potency and selectivity. One would have had a reasonable expectation of success because such analysis has been conducted for numerous divergent peptides.

Thus, the claims are rendered obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANISH GUPTA whose telephone number is (571)272-0965. The examiner can normally be reached on 5/4/9.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654